Welcome to STN International! Enter x:x

LOGINID: SSSPTA1653HXP

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

NEWS 2 AUG 10 Time limit for inactive STN sessions doubles to 40 minutes

NEWS 3 AUG 18 COMPENDEX indexing changed for the Corporate Source (CS) field

NEWS 4 AUG 24 ENCOMPLIT/ENCOMPLIT2 reloaded and enhanced

NEWS 5 AUG 24 CA/CAplus enhanced with legal status information for U.S. patents

NEWS 6 SEP 09 50 Millionth Unique Chemical Substance Recorded in CAS REGISTRY

NEWS 7 SEP 11 WPIDS, WPINDEX, and WPIX now include Japanese FTERM thesaurus

NEWS 8 OCT 21 Derwent World Patents Index Coverage of Indian and Taiwanese Content Expanded

NEWS 9 OCT 21 Derwent World Patents Index enhanced with human translated claims for Chinese Applications and Utility Models

NEWS 10 NOV 23 Addition of SCAN format to selected STN databases

NEWS 11 NOV 23 Annual Reload of IFI Databases

NEWS 12 DEC 01 FRFULL Content and Search Enhancements

NEWS 13 DEC 01 DGENE, USGENE, and PCTGEN: new percent identity feature for sorting BLAST answer sets

NEWS 14 DEC 02 Derwent World Patent Index: Japanese FI-TERM thesaurus added

NEWS 15 DEC 02 PCTGEN enhanced with patent family and legal status display data from INPADOCDB

NEWS 16 DEC 02 USGENE: Enhanced coverage of bibliographic and sequence information

NEWS EXPRESS MAY 26 09 CURRENT WINDOWS VERSION IS V8.4, AND CURRENT DISCOVER FILE IS DATED 06 APRIL 2009.

NEWS HOURS STN Operating Hours Plus Help Desk Availability NEWS LOGIN Welcome Banner and News Items

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN customer agreement. This agreement limits use to scientific research. Use for software development or design, implementation of commercial gateways, or use of CAS and STN data in the building of commercial products is prohibited and may result in loss of user privileges and other penalties.

FILE 'HOME' ENTERED AT 18:04:37 ON 11 DEC 2009

=> file medline, biosis, wpids, hcaplus, biotechds, dgene, embase, scisearch COST IN U.S. DOLLARS SINCE FILE TOTAL

FULL ESTIMATED COST

ENTRY SESSION 0.44 0.44

FILE 'MEDLINE' ENTERED AT 18:05:53 ON 11 DEC 2009

FILE 'BIOSIS' ENTERED AT 18:05:53 ON 11 DEC 2009 Copyright (c) 2009 The Thomson Corporation

FILE 'WPIDS' ENTERED AT 18:05:53 ON 11 DEC 2009 COPYRIGHT (C) 2009 THOMSON REUTERS

FILE 'HCAPLUS' ENTERED AT 18:05:53 ON 11 DEC 2009
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2009 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'BIOTECHDS' ENTERED AT 18:05:53 ON 11 DEC 2009 COPYRIGHT (C) 2009 THOMSON REUTERS

FILE 'DGENE' ENTERED AT 18:05:53 ON 11 DEC 2009 COPYRIGHT (C) 2009 THOMSON REUTERS

FILE 'EMBASE' ENTERED AT 18:05:53 ON 11 DEC 2009 Copyright (c) 2009 Elsevier B.V. All rights reserved.

FILE 'SCISEARCH' ENTERED AT 18:05:53 ON 11 DEC 2009 Copyright (c) 2009 The Thomson Corporation

=> s thrombopoietin L1 28224 THROMBOPOIETIN

=> s 11 and human
6 FILES SEARCHED...

L2 17018 L1 AND HUMAN

=> s L2 and purification

L3 1051 L2 AND PURIFICATION

=> s thrombopoietin purification

L4 7 THROMBOPOIETIN PURIFICATION

 \Rightarrow s 13 and 14

L5 7 L3 AND L4

=> d 14 ti abs ibib tot

L4 ANSWER 1 OF 7 WPIDS COPYRIGHT 2009 THOMSON REUTERS on STN

TI Thrombopoietin purification by removal of protein contaminants using hydroxyapatite - provides homogenous preparation of thrombopoietin substantially free of contaminants

AN 1997-052235 [05] WPIDS

AB WO 1996040773 A1 UPAB: 20060112

A novel method for purifying thrombopoietin (TPO) from a biological fluid comprises: (a) reducing the volume of a TPO-containing biological fluid by a method selected from the gp. consisting of ligand affinity chromatography,

ion-exchange chromatography, hydrophobic interaction chromatography and ultrafiltration to provide a concentrated fraction; (b) adjusting the salt concentration of the concentrated fraction to provide an adjusted solution; (c) acidifying the adjusted solution to precipitate contaminant proteins and provide a cleared solution; (d) fractionating the cleared solution by anion-exchange chromatography to provide a TPO-enriched fraction; (e) exposing the TPO-enriched fraction to hydroxyapatite where protein contaminants are bound to the hydroxyapatite and TPO remains substantially unbound; (f) collecting the unbound TPO; and (g) concentrating the collected TPO by cation-exchange chromatography or ultrafiltration. Also claimed is a method for removing protein contaminants from a solution comprising TPO and protein contaminants, comprising exposing the solution to hydroxyapatite, where the protein contaminants are bound to the hydroxyapatite and the TPO remains substantially unbound, and recovering the TPO.

USE - TPO prepared by the above method can be used therapeutically wherever it is desirable to increase proliferation of cells in the bone marrow, such as in the treatment of cytopenias, e.g. induced by aplastic anaemia, myelodisplastic syndromes, chemotherapy or congenital cytopenias.

Member (0003)

ABEQ EP 839158 A1 UPAB 20060112

A novel method for purifying thrombopoietin (TPO) from a biological fluid comprises: (a) reducing the volume of a TPO-contq. biological fluid by a method selected from the qp. consisting of ligand affinity chromatography, ion-exchange chromatography, hydrophobic interaction chromatography and ultrafiltration to provide a concentrated fraction; (b) adjusting the salt concn. of the concentrated fraction to provide an adjusted soln.; (c) acidifying the adjusted soln. to precipitate contaminant proteins and provide a cleared soln.; (d) fractionating the cleared soln. by anion-exchange chromatography to provide a TPO-enriched fraction; (e) exposing the TPO-enriched fraction to hydroxyapatite where protein contaminants are bound to the hydroxyapatite and TPO remains substantially unbound; (f) collecting the unbound TPO; and (g) concentrating the collected TPO by cation-exchange chromatography or ultrafiltration. Also claimed is a method for removing protein contaminants from a soln. comprising TPO and protein contaminants, comprising exposing the soln. to hydroxyapatite, where the protein contaminants are bound to the hydroxyapatite and the TPO remains substantially unbound, and recovering the TPO.

USE - TPO prepd. by the above method can be used therapeutically wherever it is desirable to increase proliferation of cells in the bone marrow, such as in the treatment of cytopenias, e.g. induced by aplastic anaemia, myelodisplastic syndromes, chemotherapy or congenital cytopenias.

Member (0004)

ABEQ US 5744587 A UPAB 20060112

A novel method for purifying thrombopoietin (TPO) from a biological fluid comprises: (a) reducing the volume of a TPO-contg. biological fluid by a method selected from the gp. consisting of ligand affinity chromatography, ion-exchange chromatography, hydrophobic interaction chromatography and ultrafiltration to provide a concentrated fraction; (b) adjusting the salt concn. of the concentrated fraction to provide an adjusted soln.; (c) acidifying the adjusted soln. to precipitate contaminant proteins and provide a cleared soln.; (d) fractionating the cleared soln. by anion-exchange chromatography to provide a TPO-enriched fraction; (e) exposing the TPO-enriched fraction to hydroxyapatite where protein contaminants are bound to the hydroxyapatite and TPO remains substantially unbound; (f) collecting the unbound TPO; and (g) concentrating the collected TPO by cation-exchange chromatography or ultrafiltration. Also claimed is a method for removing protein contaminants from a soln.

comprising TPO and protein contaminants, comprising exposing the soln. to hydroxyapatite, where the protein contaminants are bound to the hydroxyapatite and the TPO remains substantially unbound, and recovering the TPO.

USE - TPO prepd. by the above method can be used therapeutically wherever it is desirable to increase proliferation of cells in the bone marrow, such as in the treatment of cytopenias, e.g. induced by aplastic anaemia, myelodisplastic syndromes, chemotherapy or congenital cytopenias.

Member (0007)

ABEQ JP 11507033 W UPAB 20060112

A novel method for purifying thrombopoietin (TPO) from a biological fluid comprises: (a) reducing the volume of a TPO-contq. biological fluid by a method selected from the gp. consisting of ligand affinity chromatography, ion-exchange chromatography, hydrophobic interaction chromatography and ultrafiltration to provide a concentrated fraction; (b) adjusting the salt concn. of the concentrated fraction to provide an adjusted soln.; (c) acidifying the adjusted soln. to precipitate contaminant proteins and provide a cleared soln.; (d) fractionating the cleared soln. by anion-exchange chromatography to provide a TPO-enriched fraction; (e) exposing the TPO-enriched fraction to hydroxyapatite where protein contaminants are bound to the hydroxyapatite and TPO remains substantially unbound; (f) collecting the unbound TPO; and (g) concentrating the collected TPO by cation-exchange chromatography or ultrafiltration. Also claimed is a method for removing protein contaminants from a soln. comprising TPO and protein contaminants, comprising exposing the soln. to hydroxyapatite, where the protein contaminants are bound to the hydroxyapatite and the TPO remains substantially unbound, and recovering the TPO.

USE - TPO prepd. by the above method can be used therapeutically wherever it is desirable to increase proliferation of cells in the bone marrow, such as in the treatment of cytopenias, e.g. induced by aplastic anaemia, myelodisplastic syndromes, chemotherapy or congenital cytopenias.

ACCESSION NUMBER: 1997-052235 [05] WPIDS

DOC. NO. CPI: C1997-017386 [05]

TITLE: Thrombopoietin purification by

removal of protein contaminants using hydroxyapatite -

provides homogenous preparation of thrombopoietin

substantially free of contaminants

DERWENT CLASS: A96; B04; D16

INVENTOR: ALASKA A A; ALASKA A R; CHANG J; DOWNEY W; FORSTROM J W;

PHAN L; ALASKA A; FORSTROM W

PATENT ASSIGNEE: (ZYMO-C) ZYMOGENETICS INC

COUNTRY COUNT: 69

PATENT INFO ABBR.:

PATENT NO	KINI	D DATE	WEEK	LA	PG	MAIN IPC
WO 9640773	 A1	19961219	(199705)*	EN	33[0]	
AU 9658718	Α	19961230	(199716)	EN		
EP 839158	A1	19980506	(199822)	EN	[0]	
US 5744587	А	19980428	(199824)	EN	9[0]	
AU 694043	В	19980709	(199838)	EN		
NZ 308862	А	19990128	(199910)	EN		
JP 11507033	W	19990622	(199935)	JA	29	
MX 9709312	A1	19980201	(199954)	ES		
KR 99022541	А	19990325	(200023)	KO	[0]	
CA 2223236	С	20000919	(200054)	EN		
KR 255466	В1	20000501	(200128)	KO		
MX 205114	В	20011109	(200279)	ES		

CN	1187202	Α	19980708	(200336)	ZΗ
EP	839158	В1	20051228	(200605)	ΕN
DE	69635661	E	20060202	(200615)	DE
DE	69635661	Т2	20060720	(200652)	DE

APPLICATION DETAILS:

PATENT NO	KIND	API	PLICATION	DATE
WO 9640773 A1 US 5744587 A AU 9658718 A AU 694043 B CA 2223236 C CN 1187202 A DE 69635661 E EP 839158 A1 EP 839158 B1 DE 69635661 E NZ 308862 A EP 839158 A1 NZ 308862 A JP 11507033 W KR 99022541 A CA 2223236 C KR 255466 B1 CN 1187202 A EP 839158 B1 DE 69635661 E JP 11507033 W MX 9709312 A1	KIND	WO US AU AU CA CN DE EP EP NZ WO WO WO WO WO JP MX	1996-US7453 1995-484246 1996-58718 1996-58718 1996-222323 1996-194563 1996-635661 1996-920393 1996-920393 1996-920393 1996-920393 1996-US7453 1996-US7453 1996-US7453 1996-US7453 1996-US7453 1996-US7453 1996-US7453 1996-US7453 1996-US7453 1996-US7453 1996-US7453 1996-US7453 1996-US7453 1996-US7453 1996-US7453 1996-US7453 1996-US7453	19960522 19960522 19960522 6 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522
MX 205114 B		MX	1997-9312 1	9971201
MX 9709312 A1 MX 205114 B KR 99022541 A KR 255466 B1 DE 69635661 T2		MX MX KR KR DE	1997-9312 1 1997-9312 1 1997-709022 1997-709022 1996-635661	9971201 9971201 19971206 19971206 19960522
DE 69635661 T2 DE 69635661 T2			1996-920393 1996-US7453	

FILING DETAILS:

PAT	TENT NO		KIN	ID	PATENT NO	
AU	694043		В	Previous Puk	 ol AU 9658718	A
DE	6963566	61	E	Based on	EP 839158	Α
AU	9658718	3	Α	Based on	WO 9640773	Α
EP	839158		A1	Based on	WO 9640773	Α
AU	694043		В	Based on	WO 9640773	Α
NZ	308862		Α	Based on	WO 9640773	Α
JP	1150703	33	W	Based on	WO 9640773	Α
KR	990225	41	Α	Based on	WO 9640773	Α
CA	2223236	6	С	Based on	WO 9640773	Α
CN	1187202	2	Α	Based on	WO 9640773	Α
EP	839158		В1	Based on	WO 9640773	Α
DE	6963566	61	E	Based on	WO 9640773	Α
DE	6963566	51	Τ2	Based on	EP 839158	Α
DE	696356	61	T2	Based on	WO 9640773	А
PRIORITY	APPLN.	INFO:		1995-484246 1996-US7453	19950607 19960522	

TI Thrombopoietin purification by removal of protein contaminants using hydroxyapatite;
human thrombopoietin purification using hydroxyapatite chromatography

AN 1997-01852 BIOTECHDS

A method for purifying human thrombopoietin (TPO) from a biological fluid AΒ is claimed, and involves: (1) reducing the column of a TPO-containing fluid by ligand affinity chromatography, ionexchange chromatography, hydrophobic interaction chromatography and ultrafiltration to provide a concentrated fraction; (2) adjusting the salt concentration of the concentration fraction; (3) acidifying the adjusted solution to precipitate contaminant proteins and provide a cleared solution; (4) fractionating the cleared solution by anion-exchange chromatography to provide a TPO-enriched fraction; (5) exposing this fraction to hydroxyapatite chromatography so that protein contaminants remain bound to the column and the TPO remains unbound; (6) collecting the unbound TPO; and (7) concentrating the collected TPO by cation-exchange chromatography or ultrafiltration. The biological fluid is a cell-conditioned culture medium. TPO obtained by this method can be used therapeutically e.g. in the treatment of cytopenias. (33pp)

ACCESSION NUMBER: 1997-01852 BIOTECHDS

TITLE: Thrombopoietin purification by removal of protein contaminants using hydroxyapatite;

human thrombopoietin purification using hydroxyapatite chromatography

AUTHOR: Alaska A R; Chang J J; Downey W; Forstrom J W; Phan L

PATENT ASSIGNEE: Zymogenetics

LOCATION: Seattle, WA, USA.

PATENT INFO: WO 9640773 19 Dec 1996

APPLICATION INFO: WO 1996-US7453 22 May 1996

PRIORITY INFO: US 1995-484246 7 Jun 1995

DOCUMENT TYPE: Patent LANGUAGE: English

ΑN

OTHER SOURCE: WPI: 1997-052235 [05]

L4 ANSWER 3 OF 7 BIOTECHDS COPYRIGHT 2009 THOMSON REUTERS on STN

New pure thrombopoietin free of low-mol.weight degradation products;

purification from cell culture supernatant or milk by MPL receptor ligand-binding domain affinity chromatography and anion-exchange chromatography

1996-11056 BIOTECHDS

AB A new purified mammal thrombopoietin (TPO) has a mol.weight of 70,000 +/-10,000 (denaturing SDS-PAGE), is at least 90% pure as determined by SDS-PAGE and silver staining, and is free of TPO species of mol.weight less than 55,000. The TPO may be of mouse, primate or human origin, with a specified protein sequence. The TPO is purified from a conditioned cell culture supernatant or milk by an optional concentration step, affinity chromatography against a ligand-binding domain of an MPL receptor on crosslinked agarose beads, and anion-exchange chromatography. TPO stimulates megakaryocytopoiesis and thrombocytopoiesis, and may be used to increase the level of platelets in the blood, e.g. in cases of aplastic anemia, myelodysplastic syndrome, chemotherapy, congenital cytopenia, etc., and may also be used to increase the number of circulating erythrocytes (or precursors), especially in therapy of anemia associated with bone marrow failure. The new TPO preparation is homogeneous and free of proteolytic degradation products. Its use reduces the need for transfusion and thus the risk of platelet alloimmunity. (91pp)

ACCESSION NUMBER: 1996-11056 BIOTECHDS

TITLE: New pure thrombopoietin free of low-mol.weight degradation products;

purification from cell culture supernatant or milk by MPL receptor ligand-binding domain affinity chromatography and

anion-exchange chromatography
Forstrom J W; Lofton-Day C E; Lok S

AUTHOR: Forstrom J W; Lofton PATENT ASSIGNEE: Zymogenetics

LOCATION: Seattle, WA, USA.

PATENT INFO: WO 9620955 11 Jul 1996

APPLICATION INFO: WO 1995-US16626 20 Dec 1995

PRIORITY INFO: US 1994-366859 30 Dec 1994

DOCUMENT TYPE: Patent LANGUAGE: English

OTHER SOURCE: WPI: 1996-333942 [33]

L4 ANSWER 4 OF 7 BIOTECHDS COPYRIGHT 2009 THOMSON REUTERS on STN

TI Hematopoietic proteins and polypeptides; useful in in vivo and ex vivo therapy

AN 1995-13081 BIOTECHDS

A mouse or human hematopoietic protein (I) (protein sequences disclosed) AΒ stimulating the proliferation or differentiation of myeloid or lymphoid precursors is claimed. Also claimed are: proteins with at least 80% homology to (I); DNA encoding (I) (DNA sequence disclosed); DNA encoding (I), allelic variants, complementary sequences and DNA with at least 80% homology to the DNA encoding (I); the EcoRI-XhoI insert of plasmid pZGmp1-1081 (ATCC 69566) and its allelic variants; an expression vector containing a transcription promoter and a (I)-encoding DNA segment; a transformed fungus, yeast, bacterium or mammal cell culture containing the vector; a non-human transgenic animal containing the claimed DNA sequences in its germline; production of recombinant hematopoietic protein by culturing the transformed cell culture; a pharmaceutical composition of (I); an antibody; a method for stimulating platelet production in a mammal using (I); a DNA probe; a method for detecting DNA encoding thrombopoietin using the DNA probe; a method for stimulating cell proliferation using (I); and a method for thrombopoietin purification using the antibody. (137pp)

ACCESSION NUMBER: 1995-13081 BIOTECHDS

TITLE: Hematopoietic proteins and polypeptides; useful in in vivo and ex vivo therapy

AUTHOR: Holly R D; Lok S; Foster D C; Hagen F S; Kaushansky K;

Kuijper J L; Lofton-Day C; Oort P J; Burkhead S K

PATENT ASSIGNEE: Zymogenetics; Univ.Washington-Seattle

PATENT INFO: WO 9521920 17 Aug 1995 APPLICATION INFO: WO 1994-US8806 5 Aug 1994

PRIORITY INFO: US 1994-525491 1 Jun 1994; US 1994-196025 14 Feb 1994

DOCUMENT TYPE: Patent LANGUAGE: English

OTHER SOURCE: WPI: 1995-293121 [38]

L4 ANSWER 5 OF 7 BIOTECHDS COPYRIGHT 2009 THOMSON REUTERS on STN

TI Studies on the purification of thrombopoietin from kidney cell culture protein;

using ammonium sulfate fractionation and chromatography

AN 1985-10996 BIOTECHDS

AB A thrombocytopoiesis-stimulating factor (TSF) has been purified from human embryonic kidney (HEK) cell culture medium. In the initial purification step, crude HEK cell culture medium was fractionated with saturated ammonium sulfate. The proteins precipitated at 40-60% and 60-80% saturation increased the % of sulfur 35 incorporation into platelets of assay mice. These proteins were refined on Sephadex G-75 columns, and the fraction containing the highest specific activity was purified by DEAE-cellulose column chromatography. TSF activity was eluted from the columns between 0.3 and 1.0 mol/l NaCl. Additional Sephadex

chromatography of post-DEAE-chromatographic preparations further increased the purity of the TSF. TSF was further processed on a DEAE HPLC column or size exclusion (SE)-HPLC columns. After HPLC, the activity was localized in a region corresponding to a retention time of 6 to 8 min for the DEAE-HPLC, but longer times were found after SE-HPLC. TSF was further purified by additional SDS-PAGE and SE-HPLC. The final product had significant TSF activity and represented a purification of about 500,000-fold. (22 ref)

ACCESSION NUMBER: 1985-10996 BIOTECHDS

TITLE: Studies on the purification of thrombopoietin from kidney

cell culture protein;

using ammonium sulfate fractionation and chromatography

AUTHOR: McDonald T P; Cottrell M; Clift R; Khouri J A; Long M D

CORPORATE SOURCE: Abbott

LOCATION: University of Tennessee College of Veterinary Medicine, P.O.

Box 1071, Knoxville, TN 37901-1071, USA.

SOURCE: J.Lab.Clin.Med.; (1985) 106, 2, 162-74

CODEN: JLCMAK

DOCUMENT TYPE: Journal LANGUAGE: English

L4 ANSWER 6 OF 7 DGENE COPYRIGHT 2009 THOMSON REUTERS on STN

TI Thrombopoietin purification by removal of protein

contaminants using hydroxyapatite - provides homogenous preparation of thrombopoietin substantially free of contaminants

AN AAW22466 protein DGENE

AAW22465 and AAW22466 represent the mouse and human thrombopoietins AB (TPO), respectively. These sequences can be purified using the method of the invention. The method of the invention is for purifying TPO from a biological fluid. The method comprises reducing the volume of a TPO containing biological fluid to provide a concentrated fraction, adjusting the salt concentration of the fraction, and acidifying the adjusted solution to precipitate contaminant proteins. The cleared solution is fractionated to give a TPO enriched fraction. The TPO-enriched fraction is exposed to hydroxyapatite, and TPO remains substantially unbound while contaminants bind to the hydroxyapatite. The unbound TPO is collected and concentrated. TPO prepared by this method can be used therapeutically wherever it is desirable to increase proliferation of cells in the bone marrow, such as in the treatment of cytopenias, e.g. induced by aplastic anaemia, myelodisplastic syndromes, chemotherapy or congenital cytopenias.

ACCESSION NUMBER: AAW22466 protein DGENE

TITLE: Thrombopoietin purification by removal of

protein contaminants using hydroxyapatite - provides
homogenous preparation of thrombopoietin substantially free

of contaminants

INVENTOR: Alaska A R; Chang J; Downey W; Forstrom J W; Phan L

PATENT ASSIGNEE: (ZYMO)ZYMOGENETICS INC.

PATENT INFO: WO 9640773 A1 19961219 33

APPLICATION INFO: WO 1996-US7453 19960522 PRIORITY INFO: US 1995-484246 19950607

PAT. SEQ. LOC: Disclosure; Page 23-25

DOCUMENT TYPE: Patent LANGUAGE: English

OTHER SOURCE: 1997-052235 [05]
DESCRIPTION: Human thrombopoietin.

L4 ANSWER 7 OF 7 DGENE COPYRIGHT 2009 THOMSON REUTERS on STN

TI Thrombopoietin purification by removal of protein contaminants using hydroxyapatite - provides homogenous preparation of thrombopoietin substantially free of contaminants

AAW22465 protein ΑN DGENE AAW22465 and AAW22466 represent the mouse and human thrombopoietins AB (TPO), respectively. These sequences can be purified using the method of the invention. The method of the invention is for purifying TPO from a biological fluid. The method comprises reducing the volume of a TPO containing biological fluid to provide a concentrated fraction, adjusting the salt concentration of the fraction, and acidifying the adjusted solution to precipitate contaminant proteins. The cleared solution is fractionated to give a TPO enriched fraction. The TPO-enriched fraction is exposed to hydroxyapatite, and TPO remains substantially unbound while contaminants bind to the hydroxyapatite. The unbound TPO is collected and concentrated. TPO prepared by this method can be used therapeutically wherever it is desirable to increase proliferation of cells in the bone marrow, such as in the treatment of cytopenias, e.g. induced by aplastic anaemia, myelodisplastic syndromes, chemotherapy or congenital cytopenias Revised record issued on 15-JUN-2007: Enhanced with precomputed information from BOND. ACCESSION NUMBER: AAW22465 protein DGENE Thrombopoietin purification by removal of TITLE: protein contaminants using hydroxyapatite - provides homogenous preparation of thrombopoietin substantially free of contaminants Alaska A R; Chang J; Downey W; Forstrom J W; Phan L INVENTOR: PATENT ASSIGNEE: (ZYMO) ZYMOGENETICS INC. WO 9640773 A1 19961219 33 PATENT INFO: APPLICATION INFO: WO 1996-US7453 19960522 PRIORITY INFO: US 1995-484246 19950607 PAT. SEQ. LOC: Disclosure; Page 22-23 DOCUMENT TYPE: Patent LANGUAGE: English OTHER SOURCE: 1997-052235 [05] CROSS REFERENCES: PC-NCBI: gi506827 PC-SWISSPROT: P40225 DESCRIPTION: Mouse thrombopoietin. => d his (FILE 'HOME' ENTERED AT 18:04:37 ON 11 DEC 2009) FILE 'MEDLINE, BIOSIS, WPIDS, HCAPLUS, BIOTECHDS, DGENE, EMBASE, SCISEARCH' ENTERED AT 18:05:53 ON 11 DEC 2009 L1 28224 S THROMBOPOIETIN L217018 S L1 AND HUMAN T.3 1051 S L2 AND PURIFICATION 7 S THROMBOPOIETIN PURIFICATION T.4 7 S L3 AND L4 L5=> s 13 and (affinity chromatography) 17 L3 AND (AFFINITY CHROMATOGRAPHY) => s 16 and (reverse phase chromatography) 0 L6 AND (REVERSE PHASE CHROMATOGRAPHY) => s 16 and (hydrophobic interaction chromatography) 2 L6 AND (HYDROPHOBIC INTERACTION CHROMATOGRAPHY) => d 18 ti abs ibib tot ANSWER 1 OF 2 WPIDS COPYRIGHT 2009 THOMSON REUTERS on STN 1.8 TΙ Thrombopoietin purification by removal of protein

contaminants using hydroxyapatite - provides homogenous preparation of thrombopoietin substantially free of contaminants

AN 1997-052235 [05] WPIDS

AB WO 1996040773 A1 UPAB: 20060112

A novel method for purifying thrombopoietin (TPO) from a biological fluid comprises: (a) reducing the volume of a TPO-containing biological fluid by a method selected from the qp. consisting of ligand affinity chromatography, ion-exchange chromatography, hydrophobic interaction chromatography and ultrafiltration to provide a concentrated fraction; (b) adjusting the salt concentration of the concentrated fraction to provide an adjusted solution; (c) acidifying the adjusted solution to precipitate contaminant proteins and provide a cleared solution; (d) fractionating the cleared solution by anion-exchange chromatography to provide a TPO-enriched fraction; (e) exposing the TPO-enriched fraction to hydroxyapatite where protein contaminants are bound to the hydroxyapatite and TPO remains substantially unbound; (f) collecting the unbound TPO; and (g) concentrating the collected TPO by cation-exchange chromatography or ultrafiltration. Also claimed is a method for removing protein contaminants from a solution comprising TPO and protein contaminants, comprising exposing the solution to hydroxyapatite, where the protein contaminants are bound to the hydroxyapatite and the TPO remains substantially unbound, and recovering the TPO.

USE - TPO prepared by the above method can be used therapeutically wherever it is desirable to increase proliferation of cells in the bone marrow, such as in the treatment of cytopenias, e.g. induced by aplastic anaemia, myelodisplastic syndromes, chemotherapy or congenital cytopenias.

Member (0003)

ABEQ EP 839158 A1 UPAB 20060112

A novel method for purifying thrombopoietin (TPO) from a biological fluid comprises: (a) reducing the volume of a TPO-contg. biological fluid by a method selected from the gp. consisting of ligand affinity chromatography, ion-exchange chromatography, hydrophobic interaction chromatography and ultrafiltration to provide a concentrated fraction; (b) adjusting the salt concn. of the concentrated fraction to provide an adjusted soln.; (c) acidifying the adjusted soln. to precipitate contaminant proteins and provide a cleared soln.; (d) fractionating the cleared soln. by anion-exchange chromatography to provide a TPO-enriched fraction; (e) exposing the TPO-enriched fraction to hydroxyapatite where protein contaminants are bound to the hydroxyapatite and TPO remains substantially unbound; (f) collecting the unbound TPO; and (g) concentrating the collected TPO by cation-exchange chromatography or ultrafiltration. Also claimed is a method for removing protein contaminants from a soln. comprising TPO and protein contaminants, comprising exposing the soln. to hydroxyapatite, where the protein contaminants are bound to the hydroxyapatite and the TPO remains substantially unbound, and recovering the TPO.

USE - TPO prepd. by the above method can be used therapeutically wherever it is desirable to increase proliferation of cells in the bone marrow, such as in the treatment of cytopenias, e.g. induced by aplastic anaemia, myelodisplastic syndromes, chemotherapy or congenital cytopenias.

Member (0004)

ABEQ US 5744587 A UPAB 20060112

A novel method for purifying thrombopoietin (TPO) from a biological fluid comprises: (a) reducing the volume of a TPO-contg. biological fluid by a method selected from the gp. consisting of ligand affinity chromatography, ion-exchange chromatography, hydrophobic interaction chromatography and

ultrafiltration to provide a concentrated fraction; (b) adjusting the salt concn. of the concentrated fraction to provide an adjusted soln.; (c) acidifying the adjusted soln. to precipitate contaminant proteins and provide a cleared soln.; (d) fractionating the cleared soln. by anion-exchange chromatography to provide a TPO-enriched fraction; (e) exposing the TPO-enriched fraction to hydroxyapatite where protein contaminants are bound to the hydroxyapatite and TPO remains substantially unbound; (f) collecting the unbound TPO; and (g) concentrating the collected TPO by cation-exchange chromatography or ultrafiltration. Also claimed is a method for removing protein contaminants from a soln. comprising TPO and protein contaminants, comprising exposing the soln. to hydroxyapatite, where the protein contaminants are bound to the hydroxyapatite and the TPO remains substantially unbound, and recovering the TPO.

USE - TPO prepd. by the above method can be used therapeutically wherever it is desirable to increase proliferation of cells in the bone marrow, such as in the treatment of cytopenias, e.g. induced by aplastic anaemia, myelodisplastic syndromes, chemotherapy or congenital cytopenias.

Member (0007)

ABEQ JP 11507033 W UPAB 20060112

A novel method for purifying thrombopoietin (TPO) from a biological fluid comprises: (a) reducing the volume of a TPO-contg. biological fluid by a method selected from the gp. consisting of ligand affinity chromatography, ion-exchange chromatography, hydrophobic interaction chromatography and ultrafiltration to provide a concentrated fraction; (b) adjusting the salt concn. of the concentrated fraction to provide an adjusted soln.; (c) acidifying the adjusted soln. to precipitate contaminant proteins and provide a cleared soln.; (d) fractionating the cleared soln. by anion-exchange chromatography to provide a TPO-enriched fraction; (e) exposing the TPO-enriched fraction to hydroxyapatite where protein contaminants are bound to the hydroxyapatite and TPO remains substantially unbound; (f) collecting the unbound TPO; and (g) concentrating the collected TPO by cation-exchange chromatography or ultrafiltration. Also claimed is a method for removing protein contaminants from a soln. comprising TPO and protein contaminants, comprising exposing the soln. to hydroxyapatite, where the protein contaminants are bound to the hydroxyapatite and the TPO remains substantially unbound, and recovering the TPO.

USE - TPO prepd. by the above method can be used therapeutically wherever it is desirable to increase proliferation of cells in the bone marrow, such as in the treatment of cytopenias, e.g. induced by aplastic anaemia, myelodisplastic syndromes, chemotherapy or congenital cytopenias.

ACCESSION NUMBER: 1997-052235 [05] WPIDS

DOC. NO. CPI: C1997-017386 [05]

TITLE: Thrombopoietin purification by

> removal of protein contaminants using hydroxyapatite provides homogenous preparation of thrombopoietin

substantially free of contaminants

A96; B04; D16 DERWENT CLASS:

ALASKA A A; ALASKA A R; CHANG J; DOWNEY W; FORSTROM J W; INVENTOR:

PHAN L; ALASKA A; FORSTROM W
(ZYMO-C) ZYMOGENETICS INC

PATENT ASSIGNEE:

COUNTRY COUNT:

PATENT INFO ABBR.:

PATENT NO KIND DATE WEEK LA PG MAIN IPC _____ WO 9640773 A1 19961219 (199705)* EN 33[0]

AU	9658718	Α	19961230	(199716)	ΕN	
ΕP	839158	A1	19980506	(199822)	ΕN	[0]
US	5744587	Α	19980428	(199824)	ΕN	9[0]
AU	694043	В	19980709	(199838)	ΕN	
NZ	308862	Α	19990128	(199910)	ΕN	
JΡ	11507033	W	19990622	(199935)	JA	29
MX	9709312	Α1	19980201	(199954)	ES	
KR	99022541	Α	19990325	(200023)	KO	[0]
CA	2223236	С	20000919	(200054)	ΕN	
KR	255466	В1	20000501	(200128)	KO	
MX	205114	В	20011109	(200279)	ES	
CN	1187202	Α	19980708	(200336)	ZH	
ΕP	839158	В1	20051228	(200605)	ΕN	
DE	69635661	E	20060202	(200615)	DE	
DE	69635661	Т2	20060720	(200652)	DE	

APPLICATION DETAILS:

PATENT NO	KIND	APE	PLICATION	DATE
PATENT NO	KIND	WO US AU AU CA CN DE EP EP NZ WO WO WO WO WO JP MX	PLICATION 1996-US7453 1995-484246 1996-58718 1996-58718 1996-222323 1996-194563 1996-635661 1996-920393 1996-920393 1996-920393 1996-920393 1996-US7453	19960522 19950607 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522 19960522
KR 99022541 A KR 255466 B1 DE 69635661 T2		KR KR	1997-709022 1997-709022 1996-635661	19971206 19971206
DE 69635661 T2 DE 69635661 T2		EP	1996-920393 1996-US7453	19960522

FILING DETAILS:

PATENT NO	KIND		PATENT NO	
AU 694043 DE 69635661 AU 9658718 EP 839158 AU 694043	B E A A1 B	Previous Publ Based on Based on Based on Based on	AU 9658718 EP 839158 WO 9640773 WO 9640773	A A A A A
NZ 308862	A	Based on	WO 9640773	Α
JP 11507033	W	Based on	WO 9640773	Α
KR 99022541	A	Based on	WO 9640773	Α

```
WO 9640773
     CA 2223236 C
                           Based on
                                                           Α
                         Based on
                                          WO 9640773
                     A
     CN 1187202
                                                           Α
                                          WO 9640773
     EP 839158
                    B1 Based on
                                                           Α
                    E Based on
                                          WO 9640773
     DE 69635661
                                                           Α
     DE 69635661
                    T2 Based on
                                          EP 839158
                                                           Α
     DE 69635661
                    T2 Based on
                                          WO 9640773
PRIORITY APPLN. INFO: US 1995-484246
                                          19950607
                     WO 1996-US7453
                                          19960522
L8
     ANSWER 2 OF 2 BIOTECHDS COPYRIGHT 2009 THOMSON REUTERS on STN
ΤI
      Thrombopoietin purification by removal of protein
     contaminants using hydroxyapatite;
          human thrombopoietin purification using
        hydroxyapatite chromatography
     1997-01852 BIOTECHDS
ΑN
     A method for purifying human thrombopoietin (TPO)
AΒ
      from a biological fluid is claimed, and involves: (1) reducing the column
      of a TPO-containing fluid by ligand affinity
     chromatography, ionexchange chromatography, hydrophobic
      interaction chromatography and ultrafiltration to
     provide a concentrated fraction; (2) adjusting the salt concentration of
     the concentration fraction; (3) acidifying the adjusted solution to
     precipitate contaminant proteins and provide a cleared solution; (4)
      fractionating the cleared solution by anion-exchange chromatography to
     provide a TPO-enriched fraction; (5) exposing this fraction to
     hydroxyapatite chromatography so that protein contaminants remain bound
     to the column and the TPO remains unbound; (6) collecting the unbound
      TPO; and (7) concentrating the collected TPO by cation-exchange
      chromatography or ultrafiltration. The biological fluid is a
      cell-conditioned culture medium. TPO obtained by this method can be used
     therapeutically e.g. in the treatment of cytopenias. (33pp)
ACCESSION NUMBER: 1997-01852 BIOTECHDS
                 Thrombopoietin purification by removal of
TITLE:
                 protein contaminants using hydroxyapatite;
                      human thrombopoietin
                    purification using hydroxyapatite chromatography
AUTHOR:
                 Alaska A R; Chang J J; Downey W; Forstrom J W; Phan L
PATENT ASSIGNEE: Zymogenetics
LOCATION:
                 Seattle, WA, USA.
PATENT INFO:
               WO 9640773 19 Dec 1996
APPLICATION INFO: WO 1996-US7453 22 May 1996
PRIORITY INFO: US 1995-484246 7 Jun 1995
DOCUMENT TYPE:
              Patent
LANGUAGE:
                 English
OTHER SOURCE:
               WPI: 1997-052235 [05]
=> d his
     (FILE 'HOME' ENTERED AT 18:04:37 ON 11 DEC 2009)
    FILE 'MEDLINE, BIOSIS, WPIDS, HCAPLUS, BIOTECHDS, DGENE, EMBASE,
     SCISEARCH' ENTERED AT 18:05:53 ON 11 DEC 2009
L1
          28224 S THROMBOPOIETIN
L2
         17018 S L1 AND HUMAN
L3
          1051 S L2 AND PURIFICATION
             7 S THROMBOPOIETIN PURIFICATION
L4
L5
             7 S L3 AND L4
L6
            17 S L3 AND (AFFINITY CHROMATOGRAPHY)
T.7
             0 S L6 AND (REVERSE PHASE CHROMATOGRAPHY)
```

=> s 16 and (anion exchange chromatography)
L9 3 L6 AND (ANION EXCHANGE CHROMATOGRAPHY)

=> d 19 ti abs ibib tot

L9 ANSWER 1 OF 3 WPIDS COPYRIGHT 2009 THOMSON REUTERS on STN

TI Thrombopoietin purification by removal of protein contaminants using hydroxyapatite - provides homogenous preparation of thrombopoietin substantially free of contaminants

AN 1997-052235 [05] WPIDS

AB WO 1996040773 A1 UPAB: 20060112

A novel method for purifying thrombopoietin (TPO) from a biological fluid comprises: (a) reducing the volume of a TPO-containing biological fluid by a method selected from the gp. consisting of ligand affinity chromatography, ion-exchange chromatography, hydrophobic interaction chromatography and ultrafiltration to provide a concentrated fraction; (b) adjusting the salt concentration of the concentrated fraction to provide an adjusted solution; (c) acidifying the adjusted solution to precipitate contaminant proteins and provide a cleared solution; (d) fractionating the cleared solution by anion-exchange chromatography to provide a TPO-enriched fraction; (e) exposing the TPO-enriched fraction to hydroxyapatite where protein contaminants are bound to the hydroxyapatite and TPO remains substantially unbound; (f) collecting the unbound TPO; and (g) concentrating the collected TPO by cation-exchange chromatography or ultrafiltration. Also claimed is a method for removing protein contaminants from a solution comprising TPO and protein contaminants, comprising exposing the solution to hydroxyapatite, where the protein contaminants are bound to the hydroxyapatite and the TPO remains substantially unbound, and recovering the TPO.

USE - TPO prepared by the above method can be used therapeutically wherever it is desirable to increase proliferation of cells in the bone marrow, such as in the treatment of cytopenias, e.g. induced by aplastic anaemia, myelodisplastic syndromes, chemotherapy or congenital cytopenias.

Member (0003)

ABEQ EP 839158 A1 UPAB 20060112

A novel method for purifying thrombopoietin (TPO) from a biological fluid comprises: (a) reducing the volume of a TPO-contg. biological fluid by a method selected from the gp. consisting of ligand affinity chromatography, ion-exchange chromatography, hydrophobic interaction chromatography and ultrafiltration to provide a concentrated fraction; (b) adjusting the salt concn. of the concentrated fraction to provide an adjusted soln.; (c) acidifying the adjusted soln. to precipitate contaminant proteins and provide a cleared soln.; (d) fractionating the cleared soln. by anion-exchange chromatography to provide a TPO-enriched fraction; (e) exposing the TPO-enriched fraction to hydroxyapatite where protein contaminants are bound to the hydroxyapatite and TPO remains substantially unbound; (f) collecting the unbound TPO; and (g) concentrating the collected TPO by cation-exchange chromatography or ultrafiltration. Also claimed is a method for removing protein contaminants from a soln. comprising TPO and protein contaminants, comprising exposing the soln. to hydroxyapatite, where the protein contaminants are bound to the hydroxyapatite and the TPO remains substantially unbound, and recovering the TPO.

USE - TPO prepd. by the above method can be used therapeutically wherever it is desirable to increase proliferation of cells in the bone marrow, such as in the treatment of cytopenias, e.g. induced by aplastic anaemia, myelodisplastic syndromes, chemotherapy or congenital cytopenias.

Member (0004)

ABEQ US 5744587 A UPAB 20060112

A novel method for purifying thrombopoietin (TPO) from a biological fluid comprises: (a) reducing the volume of a TPO-contg. biological fluid by a method selected from the gp. consisting of ligand affinity chromatography, ion-exchange chromatography, hydrophobic interaction chromatography and ultrafiltration to provide a concentrated fraction; (b) adjusting the salt concn. of the concentrated fraction to provide an adjusted soln.; (c) acidifying the adjusted soln. to precipitate contaminant proteins and provide a cleared soln.; (d) fractionating the cleared soln. by anion-exchange chromatography to provide a TPO-enriched fraction; (e) exposing the TPO-enriched fraction to hydroxyapatite where protein contaminants are bound to the hydroxyapatite and TPO remains substantially unbound; (f) collecting the unbound TPO; and (g) concentrating the collected TPO by cation-exchange chromatography or ultrafiltration. Also claimed is a method for removing protein contaminants from a soln. comprising TPO and protein contaminants, comprising exposing the soln. to hydroxyapatite, where the protein contaminants are bound to the hydroxyapatite and the TPO remains substantially unbound, and recovering the TPO.

USE - TPO prepd. by the above method can be used therapeutically wherever it is desirable to increase proliferation of cells in the bone marrow, such as in the treatment of cytopenias, e.g. induced by aplastic anaemia, myelodisplastic syndromes, chemotherapy or congenital cytopenias.

Member (0007)

ABEQ JP 11507033 W UPAB 20060112

A novel method for purifying thrombopoietin (TPO) from a biological fluid comprises: (a) reducing the volume of a TPO-contg. biological fluid by a method selected from the gp. consisting of ligand affinity chromatography, ion-exchange chromatography, hydrophobic interaction chromatography and ultrafiltration to provide a concentrated fraction; (b) adjusting the salt concn. of the concentrated fraction to provide an adjusted soln.; (c) acidifying the adjusted soln. to precipitate contaminant proteins and provide a cleared soln.; (d) fractionating the cleared soln. by anion-exchange chromatography to provide a TPO-enriched fraction; (e) exposing the TPO-enriched fraction to hydroxyapatite where protein contaminants are bound to the hydroxyapatite and TPO remains substantially unbound; (f) collecting the unbound TPO; and (g) concentrating the collected TPO by cation-exchange chromatography or ultrafiltration. Also claimed is a method for removing protein contaminants from a soln. comprising TPO and protein contaminants, comprising exposing the soln. to hydroxyapatite, where the protein contaminants are bound to the hydroxyapatite and the TPO remains substantially unbound, and recovering the TPO.

USE - TPO prepd. by the above method can be used therapeutically wherever it is desirable to increase proliferation of cells in the bone marrow, such as in the treatment of cytopenias, e.g. induced by aplastic anaemia, myelodisplastic syndromes, chemotherapy or congenital cytopenias.

ACCESSION NUMBER: 1997-052235 [05] WPIDS

DOC. NO. CPI: C1997-017386 [05]

TITLE: Thrombopoietin purification by

removal of protein contaminants using hydroxyapatite - provides homogenous preparation of thrombopoietin

substantially free of contaminants

DERWENT CLASS: A96; B04; D16

INVENTOR: ALASKA A A; ALASKA A R; CHANG J; DOWNEY W; FORSTROM J W;

PHAN L; ALASKA A; FORSTROM W

PATENT ASSIGNEE: (ZYMO-C) ZYMOGENETICS INC

COUNTRY COUNT: 69

PATENT INFO ABBR.:

PA	TENT NO	KINI	D DATE	WEEK	LA	PG	MAIN IPC
WO	9640773	A1	19961219	(199705)*	EN	33[0]	
ΑU	9658718	А	19961230	(199716)	ΕN		
EP	839158	A1	19980506	(199822)	ΕN	[0]	
US	5744587	A	19980428	(199824)	EN	9[0]	
ΑU	694043	В	19980709	(199838)	ΕN		
ΝZ	308862	A	19990128	(199910)	EN		
JP	11507033	W	19990622	(199935)	JA	29	
MX	9709312	A1	19980201	(199954)	ES		
KR	99022541	A	19990325	(200023)	KO	[0]	
CA	2223236	С	20000919	(200054)	ΕN		
KR	255466	В1	20000501	(200128)	KO		
MX	205114	В	20011109	(200279)	ES		
CN	1187202	A	19980708	(200336)	ZH		
ΕP	839158	В1	20051228	(200605)	ΕN		
DE	69635661	E	20060202	(200615)	DE		
DE	69635661	Т2	20060720	(200652)	DE		

APPLICATION DETAILS:

PATENT NO	KIND	API	PLICATION	DATE
WO 9640773 A1		WO	1996-US7453	19960522
US 5744587 A		US	1995-484246	19950607
AU 9658718 A		AU	1996-58718	19960522
AU 694043 B		AU	1996-58718	19960522
CA 2223236 C		CA	1996-222323	6 19960522
CN 1187202 A		CN	1996-194563	19960522
DE 69635661 E		DE	1996-635661	19960522
EP 839158 A1		EP	1996-920393	19960522
EP 839158 B1		ΕP	1996-920393	19960522
DE 69635661 E		EP	1996-920393	19960522
NZ 308862 A		NZ	1996-308862	19960522
EP 839158 A1		WO	1996-US7453	19960522
NZ 308862 A		WO	1996-US7453	19960522
JP 11507033 W		WO	1996-US7453	19960522
KR 99022541 A			1996-US7453	
CA 2223236 C		WO	1996-US7453	19960522
KR 255466 B1		WO	1996-US7453	19960522
CN 1187202 A		-	1996-US7453	
EP 839158 B1			1996-US7453	
DE 69635661 E			1996-US7453	
JP 11507033 W			1997-500670	
MX 9709312 A1			1997-9312 1	
MX 205114 B			1997-9312 1	
KR 99022541 A			1997-709022	
KR 255466 B1			1997-709022	
DE 69635661 T2			1996-635661	
DE 69635661 T2			1996-920393	
DE 69635661 T2		WO	1996-US7453	19960522

FILING DETAILS:

PAT	TENT NO	KIND		PA'	TENT NO	
AU	694043	В	Previous Publ	AU	9658718	 А
DE	69635661	E	Based on	EP	839158	Α
AU	9658718	A	Based on	WO	9640773	Α

```
WO 9640773
          EP 839158 A1 Based on
                                                                                                          Α
         AU 694043 B Based on NZ 308862 A Based on JP 11507033 W Based on CA 2223236 C Based on CN 1187202 A Based on CN 200150 A Based ON CN 20
                                                                           WO 9640773
                                                                                                          Α
                                                                           WO 9640773
                                                                                                          Α
                                                                           WO 9640773
                                                                                                          Α
                                                                           WO 9640773
                                                                                                          Α
                                                                           WO 9640773
                                                                                                         Α
          CN 1187202
                                                                          WO 9640773
                                                                                                         Α
                                   B1 Based on
E Based on
                                                                           WO 9640773
          EP 839158
                                   E
          DE 69635661
                                                                           WO 9640773
          DE 69635661
                                    T2 Based on
                                                                           EP 839158
          DE 69635661
                                    T2
                                                 Based on
                                                                           WO 9640773
PRIORITY APPLN. INFO: US 1995-484246
                                                                           19950607
                                      WO 1996-US7453
                                                                           19960522
          ANSWER 2 OF 3 BIOTECHDS COPYRIGHT 2009 THOMSON REUTERS on STN
          Thrombopoietin purification by removal of protein
          contaminants using hydroxyapatite;
                   human thrombopoietin purification using
               hydroxyapatite chromatography
          1997-01852 BIOTECHDS
          A method for purifying human thrombopoietin (TPO)
          from a biological fluid is claimed, and involves: (1) reducing the column
          of a TPO-containing fluid by ligand affinity
          chromatography, ionexchange chromatography, hydrophobic
          interaction chromatography and ultrafiltration to provide a concentrated
          fraction; (2) adjusting the salt concentration of the concentration
          fraction; (3) acidifying the adjusted solution to precipitate contaminant
          proteins and provide a cleared solution; (4) fractionating the cleared
          solution by anion-exchange chromatography
          to provide a TPO-enriched fraction; (5) exposing this fraction to
          hydroxyapatite chromatography so that protein contaminants remain bound
          to the column and the TPO remains unbound; (6) collecting the unbound
          TPO; and (7) concentrating the collected TPO by cation-exchange
          chromatography or ultrafiltration. The biological fluid is a
          cell-conditioned culture medium. TPO obtained by this method can be used
          therapeutically e.g. in the treatment of cytopenias.
ACCESSION NUMBER: 1997-01852 BIOTECHDS
TITLE:
                               Thrombopoietin purification by removal of
                               protein contaminants using hydroxyapatite;
                                         human thrombopoietin
                                     purification using hydroxyapatite chromatography
AUTHOR:
                               Alaska A R; Chang J J; Downey W; Forstrom J W; Phan L
PATENT ASSIGNEE: Zymogenetics
                               Seattle, WA, USA.
LOCATION:
                        WO 9640773 19 Dec 1996
PATENT INFO:
APPLICATION INFO: WO 1996-US7453 22 May 1996
PRIORITY INFO: US 1995-484246 7 Jun 1995
DOCUMENT TYPE:
                             Patent
LANGUAGE:
                               English
                            WPI: 1997-052235 [05]
OTHER SOURCE:
          ANSWER 3 OF 3 BIOTECHDS COPYRIGHT 2009 THOMSON REUTERS on STN
          New pure thrombopoietin free of low-mol.weight degradation
          products;
                   purification from cell culture supernatant or milk by MPL
               receptor ligand-binding domain affinity
               chromatography and anion-exchange
               chromatography
          1996-11056 BIOTECHDS
          A new purified mammal thrombopoietin (TPO) has a mol.weight of
```

L9

ΤI

ΑN

AΒ

L9 ΤI

ΑN ΔR

70,000 +/- 10,000 (denaturing SDS-PAGE), is at least 90% pure as determined by SDS-PAGE and silver staining, and is free of TPO species of mol.weight less than 55,000. The TPO may be of mouse, primate or human origin, with a specified protein sequence. The TPO is purified from a conditioned cell culture supernatant or milk by an optional concentration step, affinity chromatography against a ligand-binding domain of an MPL receptor on crosslinked agarose beads, and anion-exchange chromatography. TPO stimulates megakaryocytopoiesis and thrombocytopoiesis, and may be

used to increase the level of platelets in the blood, e.g. in cases of aplastic anemia, myelodysplastic syndrome, chemotherapy, congenital cytopenia, etc., and may also be used to increase the number of circulating erythrocytes (or precursors), especially in therapy of anemia associated with bone marrow failure. The new TPO preparation is homogeneous and free of proteolytic degradation products. Its use reduces the need for transfusion and thus the risk of platelet alloimmunity. (91pp)

ACCESSION NUMBER: 1996-11056 BIOTECHDS

New pure thrombopoietin free of low-mol.weight TITLE:

degradation products;

purification from cell culture supernatant or milk by MPL receptor ligand-binding domain

affinity chromatography and anion-exchange chromatography

AUTHOR: Forstrom J W; Lofton-Day C E; Lok S

PATENT ASSIGNEE: Zymogenetics Seattle, WA, USA. LOCATION: PATENT INFO: WO 9620955 11 Jul 1996 APPLICATION INFO: WO 1995-US16626 20 Dec 1995 PRIORITY INFO: US 1994-366859 30 Dec 1994

DOCUMENT TYPE: Patent English LANGUAGE:

OTHER SOURCE: WPI: 1996-333942 [33]